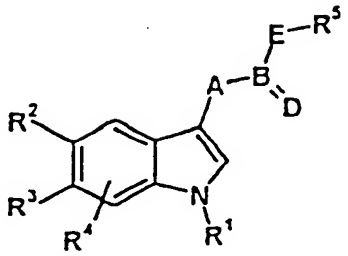
We claim:

1. A compound of the Formula



(1)

and their pharmaceutically acceptable salts, wherein

R^1, R^5 are independently of each other

(i) a C_{1-2} alkyl, straight-chain or branched-chain, optionally mono- or polysubstituted by -OH, -SH, $-NH_2$, $-NHC_{1-6}$ alkyl, $-N(C_{1-6}\ alkyl)_2$, $-NHC_{6-14}$ aryl, $-N(C_{6-14}\ aryl)_2$, $-N(C_{1-6}\ alkyl)(C_{6-14}\ aryl)$, $-NHCOR^6$, $-NO_2$, -CN, -F, -Cl, -Br, -I, $-O-C_{1-6}$ alkyl, $-O-C_{6-14}$ aryl, $-O(CO)R^6$, $-S-C_{1-6}$ alkyl, $-S-C_{6-14}$ aryl, $-SOR^6$, $-SO_3H$, $-SO_2R^6$, $-OSO_2C_{1-6}$ alkyl, $-OSO_2C_{6-14}$ aryl, $-(CS)R^6$, -COOH, $-(CO)R^6$, mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring members, mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and S, where the C_{6-14} aryl groups and the included carbocyclic and heterocyclic substituents can optionally be mono- or polysubstituted by R^4,

(ii) $-C_{2-12}$ alkenyl, mono- or polyunsaturated, straight-chain or branched-chain, optionally mono- or polysubstituted by -OH, -SH, $-NH_2$, $-NHC_{1-6}$ alkyl, $-N(C_{1-6}\ alkyl)_2$, $-NHC_{6-14}$ aryl, $-N(C_{6-14}\ aryl)_2$, $-N(C_{1-6}\ alkyl)(C_{6-14}\ aryl)$, $-NHCOR^6$, $-NO_2$, -CN, -F, -Cl, -Br, -I, $-O-C_{1-6}$ alkyl, $-O-C_{6-14}$ aryl, $-O(CO)R^6$, $-S-C_{1-6}$ alkyl, $-S-C_{6-14}$ aryl, $-SOR^6$, -SO3H, $-SO_2R^6$, $-OSO_2C_{1-6}$ alkyl, $-OSO_2C_{6-14}$ aryl, $-(CS)R^6$, -COOH, $-(CO)R^6$, mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring members, mono-, bi- or

tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and S, where the C_{6-14} aryl groups and the included carbocyclic and heterocyclic substituents for their part can optionally be mono- or polysubstituted by R^4,

(iii) mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring members, optionally mono- or polysubstituted by -OH, -SH, $-NH_2$, $-NHC_{1-6}$ alkyl, $-N(C_{1-6}$ alkyl$)_2$, $-NHC_{6-14}$ aryl, $-N(C_{6-14}$ aryl$)_2$, $-N(C_{1-6}$ alkyl$)(C_{6-14}$ aryl), $-NHCOR^6$, $-NO_2$, -CN, -F, -Cl, -Br, -I, $-O-C_{1-6}$ alkyl, $-O-C_{6-14}$ aryl, $-O(CO)R^6$, $-S-C_{1-6}$ alkyl, $-S-C_{6-14}$ aryl, $-SOR^6$, $-SO_3H$, $-SO_2R^6$, $-OSO_2C_{1-6}$ alkyl, $-OSO_2C_{6-14}$ aryl, $-(CS)R^6$, -COOH, $-(CO)R^6$, mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring members, mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and S, where the C_{6-14} aryl groups and the included carbocyclic and heterocyclic substituents can optionally be mono- or polysubstituted by R^4,

(iv) mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and S, optionally mono- or polysubstituted by -OH, -SH, $-NH_2$, $-NHC_{1-6}$ alkyl, $-N(C_{1-6}$ alkyl$)_2$, $-NHC_{6-14}$ aryl, $-N(C_{6-14}$ aryl$)_2$, $-N(C_{1-6}$ alkyl$)(C_{6-14}$ aryl), $-NHCOR^6$, $-NO_2$, -CN, -F, -Cl, -Br, -I, $-O-C_{1-6}$ alkyl, $-O-C_{6-14}$ aryl, $-O(CO)R^6$, $-S-C_{1-6}$ alkyl, $-S-C_{6-14}$ aryl, $-SOR^6$, $-SO_3H$, $-SO_2R^6$, $-OSO_2C_{1-6}$ alkyl, $-OSO_2C_{6-14}$ aryl, $-(CS)R^6$, -COOH, $-(CO)R^6$, mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring members, mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and S, where the C_{6-14} aryl groups and the included carbocyclic and heterocyclic substituents for their part can be optionally mono- or polysubstituted by R^4, -carbo- or heterocyclic saturated or mono- or

polyunsaturated spirocycles having from 3 to 10 ring members, where heterocyclic systems contains from 1 to 6 heteroatoms, which are suitably N, O and S, optionally mono- or polysubstituted by -OH, -SH, $-NH_2$, $-NHC_{1-6}$ alkyl, $-N(C_{1-6}$ alkyl$)_2$, $-NHC_{6-14}$ aryl, $-N(C_{6-14}$ aryl$)_2$, $-N(C_{1-6}$ alkyl$)(C_{6-14}$ aryl), $-NHCOR^6$, $-NO_2$, -CN, -F, -Cl, -Br, -I, $-O-C_{1-6}$ alkyl, $-O-C_{6-14}$ aryl, $-O(CO)R^6$, $-S-C_{1-6}$ alkyl, $-S-C_{6-14}$ aryl, $-SOR^6$, -SO3H, $-SO_2R^6$, $-OSO_2C_{1-6}$ alkyl, $-OSO_2C_{6-14}$ aryl, $-(CS)R^6$, -COOH, $-(CO)R^6$, mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring members, mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and S, where the C_{6-14} aryl groups and the included carbocyclic and heterocyclic substituents can optionally be mono- or polysubstituted by R^4,

R^2, R^3 are hydrogen or -OH, where at least one of the two substituents must be -OH;

R^4 is -H, -OH, -SH, $-NH_2$, $-NHC_{1-6}$ alkyl, $-N(C_{1-6}$ alkyl$)_2$, $-NHC_{6-14}$ aryl, $-N(C_{6-14}$ aryl$)_2$, $-N(C_{1-6}$ alkyl$)(C_{6-14}$ aryl), $-NHCOR^6$, $-NO_2$, -CN, -COOH, $-(CO)R^6$, $-(CS)R^6$, -F, -Cl, -Br, -I, $-O-C_{1-6}$ alkyl, $-O-C_{6-14}$ aryl, $-O(CO)R^6$, $-S-C_{1-6}$ alkyl, $-S-C_{6-14}$ aryl, $-SOR^6$, $-SO_2R^6$.

R^6 is -H, $-NH_2$, $-NHC_{1-6}$ alkyl, $-N(C_{1-6}$ alkyl$)_2$, $-NHC_{6-14}$ aryl, $-N(C_{6-14}$ aryl$)_2$, $-N(C_{1-6}$ alkyl$)(C_{6-14}$ aryl), $-O-C_{1-6}$ alkyl, $-O-C_{6-14}$ aryl, $-S-C_{1-6}$ alkyl, $-S-C_{6-14}$ aryl, $-C_{1-12}$ alkyl, straight-chain or branched-chain, $-C_{2-12}$ alkenyl, mono- or polyunsaturated, straight-chain or branched-chain, -mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring members, -mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and S;

A is either a bond, or $-CH2)_m-$, $-(CH2)_m-(CH=CH)_n-(CH_2)_p-$, $-(CHOZ)_m-$, -(C=O)-, -(C=S)-, -(C=N-Z)-, -O-, -S-, -NZ-, where m and p are cardinal numbers from 0 to 3 and n is a cardinal number from 0 to 2,

Z is H, or a C_{1-12} alkyl, straight-chain or branched-chain, C_{2-12} alkenyl, mono- or polyunsaturated, straight-chain or branched-chain, mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having from 3 to 14 ring members, mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having from 5 to 15 ring members and from 1 to 6 heteroatoms, which are suitably N, O and S;

B is either carbon or sulfur, or -(S=O)-;

D is oxygen, sulfur, CH_2 or N-Z, where D can only be S or CH_2 if B is carbon;

E is a bond, or $(CH2)_m$-, -O-, -S-, -(N-Z)-, where m and Z have the same meanings as above.

2. The compound of claim 1, wherein the compound is a pharmaceutically acceptable salt of an organic or inorganic acid, or of an organic or inorganic base, or a quaternary ammonium salt from the quaternization of a tertiary amine.

3. The compound of claim 1, having an asymetric carbon atom by being the L or the D form, or a D,L mixture, and when in a diastereoisomeric form.

4. A compound of claim 1, being one of the following compounds:

N-(3,5-dichloropyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]-2-oxoacetamide;

N-(3,5-dichloropyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]-2-oxoacetamide Na salt;

N-(3,5-dichloropyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]-2-hydroxyacetamide;

N-(pyridin-4-yl)-2-[1-2,6-difluorobenzyl)-5-hydroxyindol-3-yl]-2-oxyacetamide;

N-(3,5-dichloropyridin-4-yl)-2-[1-(2,6-difluorobenzyl)-5-hydroxyindol-3-yl]-2-oxoacetamide;

N-(3,5-dichloropyridin-4-yl)-2-[1-(3-nitrobenzyl)-5-hydroxyindol-3-yl]-2-oxoacetamide Na salt;

N-(3,5-dichloropyridin-4-yl)-2-(1-propyl-5-hydroxyindol-3-yl)-2-oxyacetamide;

N-(3,5-dichloropyridin-4-yl)-2-(1-isopropyl-5-hydroxyindol-3-yl)-2-oxoacetamide;

N-(3,5-dichloropyridin-4-yl)-2-(1-cyclopentylmethyl-5-hydroxyindol-3-yl)-2-oxoacetamide;

N-(2,6-dichlorophenyl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl]-2-oxoacetamide;

N-(2,6-dichloro-4-trifluoromethylphenyl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl)-2-oxoacetamide;

N-(2,6-dichloro-4-trifluoromethoxylphenyl)-2-[1-(4-fluorobenzyl)-5-hydroxyindol-3-yl)-2-oxoacetamide;

N-(3,5-dichloropyridin-4-yl)-2-[1-(4-fluorobenzyl)-6-hydroxyindol-3-yl]-2-oxoacetamide;

N-(3,5-dichloropyridin-4-yl)-5-hydroxy-1-(4-methoxybenzyl)indole-3-carboxamide.

5. A process for preparing compounds of claim 1, which comprises converting a compound of claim 1 wherein R_1 or R^3, or R^2 and R^3 is -O-R^7 in which R^7 is a leaving group.

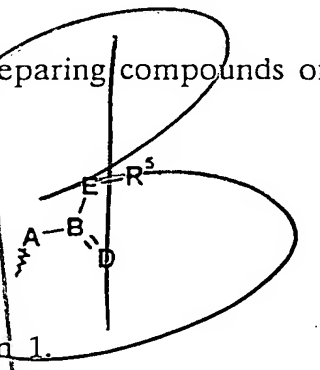
6. The process of claim 5, wherein said leaving group is alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl, acyl, alkoxycarbonyl, aryloxycarbonyl,

aminocarbonyl, N-substituted aminocarbonyl, silyl or sulfonyl residue or a complexing agent.

7. The process of claim 6, wherein said complexing agent is a compound of boric acid or phosphoric acid, or a compound containing a covalently bonded metal.

8. The process of claim 7, wherein said metal is zinc, aluminum, or copper.

9. A process for preparing compounds of claim 1, which comprises converting the substructure



into another compound of claim 1.

10. A process for inhibiting TNFα by administering to a patient in need therefor an effective amount of the compound of claim 1.

11. A process for inhibiting TNFα by administering to a patient in need therefor an effective amount of the compound of claim 4.

12. A process for inhibiting phosphodiesterase 4 by administering to a patient in need therefor an effective amount of the compound of claim 1.

13. A process for inhibiting phosphodiesterase 4 by administering to a patient in need therefor an effective amount of the compound of claim 4.

14. A process for treating an eosinophil-related condition by administering to a patient in need therefor an effective amount of the compound of claim 1.

15. A process for treating an eosinophil-related condition by administering to a patient in need therefor an effective amount of the compound of claim 4.

16. A process for treating a chronic obstructive pulmonary disease, which comprises administering to a patient in need therefor an effective amount of a compound of claim 1.

17. A process for treating a chronic obstructive pulmonary disease, which comprises administering to a patient in need therefor an effective amount of a compound of claim 4.

18. A process for treating arthritis, rheumatoid arthritis, spondylitis, osteoarthritis, sepsis, septic shock, gram negative sepsis, toxic shock syndrome, respiratory distress syndrome, asthma, chronic pulmonary disorders, bone resorption diseases, transplant rejection reactions, autoimmune disorders, lupus erythematosus, multiple sclerosis, glomerulonephritis, uveitis, insulin dependent diabetes mellitus, chronic demyelinization, malaria, infection-related fever, infection-related myalgia, AIDS, cachexia, bronchial asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, eczema, allergic angiitis, eosinophilic fasciitis, eosinophilic pneumonia, pulmonary

infiltration with eosinophilia, urticaria, ulcerative colitis, Crohn's disease, psoriasis, keratosis, pulmonary neutrophilic infiltration, chronic obstructive pulmonary disease, senile dementia, loss of memory, Parkinson's disease, depression, stroke, intermittent claudication, benign prostate hyperplasia, pollakuria, nycturia, bladder atony, kidney stone colics, and analgesic dependency, which comprises administering to a patient a pharmacologically effective amount of a compound of claim 1.

19. A pharmaceutical preparation which comprises a therapeutically effective amount of the compound of claim 1, together with one or more of a pharmaceutically acceptable carrier, diluent, and auxiliary ingredient.

20. A process for preparing the pharmaceutical preparation of claim 12, which comprises preparing a pharmaceutically acceptable dosage form from a compound of claim 1, and from one or more of a pharmaceutically acceptable carrier, diluent, and auxiliary ingredient.